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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/541,073	06/29/2005	Yoshiyuki Ishikura	47237-0561	4059

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EXAMINER	
KUDLA, JOSEPH S	

ART UNIT	PAPER NUMBER
1611	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/541,073	ISHIKURA ET AL.	
	Examiner	Art Unit	
	Joseph S. Kudla	1611	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 October 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2-11 and 28* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2-11 and 28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *07/11/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Priority

1. This application is a national stage filing under 35 U.S.C. 371 of International Application PCT/JP2004/016351 filed on October 28, 2004, which claims priority from Japanese Application No. 2003-369147 filed October 29, 2003. Priority is acknowledged.

Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Election/Restrictions

2. Applicant elects Group VI, **without** traverse, which encompasses amended claims 2-11 and 28 in Applicants' October 30, 2007 correspondence. The inventions contained within the claims in groups I-V are cancelled, encompassing claims 1 and 12-27. In summation, claims 2-11 and 28 are submitted for examination.

3. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Information Disclosure Statement

4. The Information Disclosure Sheet (IDS) correspondence submitted by Applicant on July 11, 2006 is acknowledged. The IDS has been reviewed. All references have been reviewed.

Specification

Abstract

5. The abstract of the disclosure is objected to because the abstract improperly implies that diseases states of the circulatory system are always a result of the "aging" of a subject. Disease states, especially those having etiologies and pathophysiological manifestations as complex as the circulatory system, can happen for a variety of reasons and have a greater likelihood the longer a subject lives; however, "aging" of an individual is not one of them.

Correction is required.

Drawings

6. The drawings are objected to because figure 1 appears to demonstrate that the arachidonic acid triglyceride compound administered to the rat has no greater relaxation effect than a rat not being administered the arachidonic acid triglyceride compound. To see this, notice that the origin of the line representing the rats being administered the arachidonic acid triglyceride compound does not start at zero. The line appears translated upwards to appear to give the needed results. The Examiner asks for

clarification of this issue. Corrected drawing sheets in compliance with 37 CFR 1.121(d) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. The figure or figure number of an amended drawing should not be labeled as "amended." If a drawing figure is to be canceled, the appropriate figure must be removed from the replacement sheet, and where necessary, the remaining figures must be renumbered and appropriate changes made to the brief description of the several views of the drawings for consistency. Additional replacement sheets may be necessary to show the renumbering of the remaining figures. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d). If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

Claim Objections

7. Claim 7, 8 and 9 are objected to for the following informalities: Claim 7 incorrectly uses term "symptom" referring to the drop in elasticity of the blood vessels as the result of aging. A symptom is a medical sign of a disease state that is observed by a medical practitioner during an examination. A physician would not be able to detect the symptom of a drop in elasticity of the blood vessel, but would rather detect an elevation

of blood pressure from the normotensive state for that subject. Likewise, in claim 8, Applicant refers to arteriosclerosis as a symptom of the ischemic cardiac disease state. Arteriosclerosis is a disease state that originates from inflammation of arterial walls that result in tears in the arterial lining and then subsequent deposition of metabolic wastes, cholesterol, fatty materials and unusable calcium on the arterial walls. Similarly, in claim 9, Applicant refers to angina as a disease state. Angina is a symptom of an underlying heart problem, most commonly a symptom of coronary heart disease, that is present as chest pain or discomfort that occurs when the heart muscle does not get enough oxygen-rich blood.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claim 7-11 and 28 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification fails to provide adequate written description for the term "aging." The term "aging" is not adequately defined. Applicant has failed to provide any disclosure as to what Applicants contemplate "aging" is. In the normal art context, "aging" could simply mean a reference point at a later date from a previous reference point, or a change in an organism over time. By this standard, claims 7-11 and 28 incorrectly imply or indicate that any aging of blood vessels may result in the disease states of arteriosclerosis and ischemic heart disease or the symptom angina. None of the symptoms and diseases is a result of aging, but symptoms, and diseases have a greater preponderance to occur in an "aged" subject.

9. Claims 2-11 and 28 are rejected under 35 U.S.C. 112, first paragraph, because the specification does not reasonably provide enablement for:

a) the prevention of symptoms due to aging or diseases of the circulatory system, brain and heart;

b) the use of a composition of both arachidonic acid and the triglyceride compound containing arachidonic acid;

c) the treatment of arteriosclerosis in a subject that has the symptoms of angina or the diseases of ischemic cardiac disease or cerebral apoplexy;

and

d) the treatment of a drop in elasticity in a blood vessel ;

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims without undue experimentation to treat diseases of the circulatory system.

Undue experimentation is a conclusion reached by weighing the noted factual considerations set forth below as seen in *In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)*. A conclusion of lack of enablement means that, based on the evidence regarding a fair evaluation of an appropriate combination of the factors below, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation.

These factors include:

(A) The breadth of the claims;

(B) The nature of the invention;

(C) The state of the prior art;

(D) The level of one of ordinary skill;

(E) The level of predictability in the art;

(F) The amount of direction provided by the inventor;

(G) The existence of working examples; and

(H) The quantity of experimentation needed to make or use the invention

based on the content of the disclosure.

The breadth of the claims

The breadth of the instant claims is extremely broad in scope for the types of diseases that can be prevented or treated with the composition of arachidonic acid and a triglyceride compound containing arachidonic acid. Applicant has not provided sufficient evidence to support a claim set drawn to preventing or treating circulatory, cerebral and cardiac diseases outlined in the instant claim set with the composition having arachidonic acid and a triglyceride compound containing arachidonic acid. The breadth of the claims exacerbates the complex nature of the subject matter to which the present claims are directed.

The nature of the invention

The instant claim set outlines an invention that prevents or treats circulatory, cerebral and cardiac diseases with a composition of arachidonic acid and a triglyceride compound containing arachidonic acid. The instant claim set additionally outlines that the triglyceride compound containing arachidonic acid has a special spatial location in the triglyceride (2-position), has component fatty acids of defined length in the 1,3-position and is extracted from microorganisms that are capable of producing the triglyceride.

The state of the prior art

Prior art in the field shows it is known that arachidonic acid is able to "induce a dose-dependent decrease in spontaneous contraction rate" which can protect from ischemia (Mackay et al., "Arachidonic acid protects neonatal rat cardiac myocytes from ischemic injury through ε protein kinase C," 2001, Cardiovascular Research, volume 50, pages 65-74, Abstract and cited by Applicant). However, the prior art is silent on the ability of arachidonic acid to treat or prevent arteriosclerosis with any ischemic cardiac disease or cerebral apoplexy *and* to increase the elasticity of a blood vessel.

The level of predictability in the art

The instant claimed invention is highly unpredictable. Due to the general unpredictability in the pharmaceutical art and the lack of prior art showing the effects of arachidonic acid on arteriosclerosis, Applicant would need to show evidence of the likelihood that the arachidonic acid would have the desired physiological response through examples or scholarly discussion showing the nexus between what is commonly known in the art and that which Applicant asserts is his invention. In this particular case, the arachidonic acid is required to be assessed for physiological activity by *in vivo* screening to determine if the arachidonic exhibits the desired pharmacological activity of treating or preventing the arteriosclerosis.No st udies were performed by Applicant. The prior art is silent and the discussion by Applicant to the feasibility of using arachidonic acid to treat arteriosclerosis, leads one of ordinary skill in the art to believe

the invention is speculation. Furthermore, the studies that were conducted consisted of treating rats with a triglyceride of arachidonic acid (Examples 1 and 2, pages 21 and 23 of the instant specification, respectively), not a composition of arachidonic acid and a compound having arachidonic acid as a component fatty acid. Therefore, one cannot predict the ability of the composition to elicit *any* pharmacological response, because the composition was neither exemplified in Applicants' specification nor shown in the prior art. In addition, one of ordinary skill in the art cannot predict if arachidonic acid is effective at restoring the elasticity of blood vessels, because the parameter that was actually determined was relaxation reaction (Examples 1 and 2, pages 21 and 23 of the instant specification, respectively) and relaxation rate (figures 1 and 3). Neither parameter demonstrates elasticity, which is a bidirectional parameter. Elasticity could have been shown adding acetylcholine and observing the change (expansion), then, washing the tissue to remove the acetylcholine and observing the change (contraction). Applicant is reminded of the decision *Genentech Inc. vs. NovaNordisk* which states, " [A] patent is not a hunting license. It is not a reward for a search but a compensation for its successful conclusion and 'patent protection' is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable" (42 USPQ 2d 1001, Fed. Circuit 1997).

In addition, to prevent, as defined by Merriam-Webster Dictionary is to keep from happening or existing, which implies taking advance measures against something possible or probable. Furthermore, the definition of "to prevent" and the "act of preventing" embraces the complete 100% inhibition. Thus, the burden of enablement in

the assertion of this claim is much higher than would be the case of enabling the treatment of the condition and is not achieved. Nowhere in the prior art or instant application have the compounds in the instant claim set been enabled to prevent or completely control circulatory, cerebral or cardiac diseases with arachidonic acid.

The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic regimen for the treatment of circulatory, cerebral or cardiac diseases with arachidonic acid on its face. *In re Fisher, 427 F. 2d, 833, 166 USPQ 18 (CCPA 1970)*, indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. Hence, one of skill in the art is unable to fully predict the ability of the arachidonic acid composition to treat circulatory, cerebral or cardiac diseases which Applicant claims as his invention.

The amount of direction provided by the inventor and the existence of working examples

The instant specification does not provide adequate guidance, which would allow the skilled artisan to extrapolate from the disclosure and examples provided, to practice the claimed methods commensurate in the scope with the instant claims. Applicant provides *no* guidance using the arachidonic acid composition as specified in instant claim 1, *no* guidance demonstrating the ability of arachidonic acid composition to prevent circulatory, cerebral or cardiac diseases, *no* guidance demonstrating the restoration of blood vessel elasticity and *no* guidance demonstrating the ability of

arachidonic acid composition to treat arteriosclerosis. Adequate enablement requires more than a mere statement that a compound treats a given disease.

A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation (*In re Wright, 999 F. 2d 1557, 1562; 27 USPQ 2d 1510, 1514 (Fed. Cir. 1993)*). The specification lacks sufficient disclosure to support applicant's claims of a method to treat circulatory, cerebral or cardiac diseases with the arachidonic acid composition. There is not seen sufficient working examples or data from references in the prior art providing a nexus between that which applicant asserts supporting a method of treating circulatory, cerebral or cardiac diseases with the arachidonic acid composition.

The quantity of experimentation needed to make and use the invention based on the content of the disclosure

Based on the unpredictable nature of the invention, the state of the prior art and the breadth of the claims, one skilled in the art could not use the claimed invention without undue experimentation. The essential element towards the validation of a therapeutic modality capable of performing the mechanism of action is the ability to test the compound within *specific parameters* in advance of administration of a compound and, while maintaining experimental control, link those results with sampling time points. Once it can be documented that the compound of interest elicits a desired

pharmacological response within experimental controls, the compound, for the sake of this forum, could generally be assumed to have that pharmacological activity.

Based on the unpredictable nature of the invention, the state of the prior art and the extreme breadth of the claims, one skilled in the art could not use the claimed invention without undue experimentation.

10. Claim 8 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The term "aging" is a relative term which renders the claim indefinite. The term "aging" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

11. Claims 5 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 5 refers to the "a triglyceride including at least 5% of a triglyceride with a medium-chain fatty acid bonded to the 1,3-position" which renders the claim indefinite. It is unclear from this context if the 95% of the remaining triglyceride is in some other form (perhaps arachidonic acid bonded to the other positions) *or* some other unmentioned

substituent is attached at the 1,3-position *or* whether the other 95% could be a triglyceride without or having multiple arachidonic acid substituents.

12. Claims 3 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 3 refers to "the ratio of the arachidonic acid in the total fatty acids comprising the triglyceride is at least 20%" which renders the claim indefinite. It is unclear to what ratio Applicant is referring.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

13. Claims 2-6, 10-11 and 28 are rejected under 35 U.S.C. 102(e) as being anticipated by Akimoto et al. (U.S. Patent Application Publication US 2004/0266874).

Akimoto et al. teach the use of a composition of arachidonic acid and compound having arachidonic acid as a constituent fatty acid to ameliorate the diseases caused by

decreased brain function (reference claim 1), which includes cerebrovascular dementia (page 3 column 1, line 3). The definition of cerebrovascular dementia (Strub, "Vascular Dementia," 2003, Southern Medical Journal, Volume 96, Number 4, pages 363-366, Historical Perspective Section) is an arteriosclerotic dementia in which the arteriosclerosis (hardening of the arteries) of the brain would result in a subsequent narrowing of the arteries, resulting in multiple small vessel infarcts that manifest themselves in dementia of the subject. Akimoto et al. teach the compound having arachidonic acid as the constituent fatty acid is an alcohol ester or a triglyceride or a phospholipid (as required by instant claim 2 and within reference claim 2). Example 7 on page 11 teaches the triglyceride composition is 32%. Akimoto et al. teach the triglyceride having arachidonic acid as a constituent fatty acid is extracted from multiple microorganisms (reference claim 4 and page 4, paragraph 32). The location and the identity of the medium-chain fatty acids are taught in reference claims 3 and 4, page 11. Akimoto et al. teach the preferred location of the triglyceride having arachidonic acid as a constituent fatty acid in reference claim 3, page 11.

No claims are allowed.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph S. Kudla whose telephone number is (571) 270-3288. The examiner can normally be reached on 9am - 5pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, can be reached on (571) 272-8373. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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